

538,820
 Rec'd PCT/PTO 13 JUN 2005

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
 Organization
 International Bureau



(43) International Publication Date
 1 July 2004 (01.07.2004)

PCT

(10) International Publication Number
WO 2004/054357 A1

(51) International Patent Classification⁷: **A01K 67/027**,
 C12N 15/00, 5/00, C07H 21/02, 21/04

(21) International Application Number:
 PCT/US2003/039516

(22) International Filing Date:
 12 December 2003 (12.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
 10/319,221 13 December 2002 (13.12.2002) US
 60/434,318 17 December 2002 (17.12.2002) US

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(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **METHODS AND VECTORS FOR MAKING KNOCKOUT ANIMALS**

(57) Abstract: The present invention includes methods for integrating a modifying polynucleotide into a target polynucleotide in a cell, for instance, a fish cell or a mouse cell, and methods for making chimeric animals, heterozygous animals, and homozygous animals that are chimeric, heterozygous, or homozygous, respectively, for a modifying polynucleotide integrated into a target polynucleotide. The present invention also includes vectors and methods of using the vectors for integrating a modifying polynucleotide into a target polynucleotide in a cell, for instance, a fish cell or a mouse cell.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/39516

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A01K 67/027; C12N 15/00; C12N 5/00; C07H 21/02; C07H 21/04

US CL : 800/20; 800/24; 435/325; 536/23.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 800/20; 800/24; 435/325; 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LAI et al. Production of alpha-1-3-galactosyltransferase knockout pigs by nuclear transfer cloning. Science, 08 February 2002, Vol. 295, pages 1089-1092, specifically paragraph bridging col 1-2 on page 1090 and Fig. 1.	1-10 and 16-21
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Y	HONG et al. Production of medakafish chimeras from a stable embryonic stem cell line. PNAS, March 1998, Vol. 95, pages 3679-3684.	11,13,15
Y	LEE et al. Cloned zebrafish by nuclear transfer from long-term-cultured cells. Nature Biotechnology, August 2002, Vol. 20, pages 795-799.	1-10 and 16-21
Y	WAKAMATSU et al. Fertile and diploid nuclear transplants derived from embryonic cells of a small laboratory fish medaka (Oryzias latipes). PNAS, 30 January 2001, Vol. 98, No. 3, pages 1071-1076.	1,2,4-10 and 16-21
Y	JESUTHASAN, S. Zebrafish in the spotlight. Science, 30 August 2002, Vol. 297, see page 1484, column 2, 2nd para.	1-10 and 16-21
Y	CAPECCHI, M.R. How close are we to implementing gene targeting in animals other than the mouse? PNAS, 1 February 2000, Vol. 97, No. 3, pages 956-957.	1-10 and 16-21



Further documents are listed in the continuation of Box C.



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Date of the actual completion of the international search

26 February 2004 (26.02.2004)

Date of mailing of the international search report

28 MAY 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
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INTERNATIONAL SEARCH REPORT

PCT/US03/39516

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Categ-	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CAPECCHI, M.R. The new mouse genetics: Altering the genome by gene targeting. TIG, March 1989, Vol. 5, No. 3, pages 70-76.	22-25
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Y		2